Safety Data Sheet

N-Hydroxy-2-acetylaminofluorene

Division of Safety
National Institutes
of Health

WARNING!

THIS COMPOUND IS CARCINOGENIC, MUTAGENIC, AND MODERATELY TOXIC. AVOID FORMATION AND BREATHING OF AEROSOLS.

LABORATORY OPERATIONS SHOULD BE CONDUCTED IN A FUME HOOD, GLOVE BOX, OR VENTILATED CABINET.

AVOID SKIN CONTACT: IF EXPOSED, WASH WITH SOAP AND WATER.

FOR EYE EXPOSURE, IRRIGATE IMMEDIATELY WITH LARGE AMOUNTS OF WATER. FOR INGESTION, INDUCE VOMITING. FOR INHALATION, REMOVE VICTIM PROMPTLY TO CLEAN AIR. ADMINISTER RESCUE BREATHING IF NECESSARY. REFER TO PHYSICIAN.

IN CASE OF LABORATORY SPILL, WEAR PROTECTIVE CLOTHING DURING CLEANUP. AVOID SKIN CONTACT OR BREATHING OF AEROSOLS. USE DILUTE ALKALI TO DISSOLVE COMPOUND. WASH DOWN AREA WITH SOAP AND WATER. DISPOSE OF WASTE SOLUTIONS AND MATERIALS APPROPRIATELY.

A. Background

N-Hydroxy-2-acetylaminofluorene (N-OH-AAF) has no known use other than for basic research in carcinogenesis, mutagenesis, and DNA repair. It has moderate acute toxicity for rodents and is a potent carcinogen for rodents. It is mutagenic for bacteria, especially in the presence of a metabolizing system.

B. Chemical and Physical Data

1. Chemical Abstract No.: 53-95-2

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This data sheet is provided by the Division of Safety, NIH, to accompany the *NIH Guidelines for the Laboratory Use of Chemical Carcinogens*. The information included in this document is believed to be current and accurate, but no warranty is expressed or implied.

N-OH-AAF N-Hydroxy-2-acetylaminofluorene

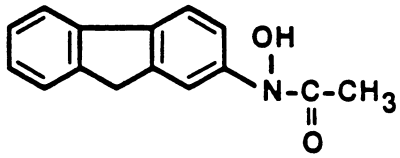
NOHAAF N-Fluoren-2-yl-acetohydoxamic a

N-Hydroxy-2-acetamidofluorene N-Hydroxy-N-(2-fluorenyl)-aceta

N-9H-Fluoren-2-yl-N-hydroxyacetamide (9CI)

Molecular formula: $C_{15}H_{13}NO_2$

structure:



weight: 239.29

Density: No data.

Absorption spectroscopy: UV: λ = 287.

Volatility: Essentially nonvolatile.

Solubility: Insoluble in water at neutrality; soluble in dilute alkali, dimethylsulfoxide, acetone, and other organic solvents.

Description, appearance: White crystalline solid.

Melting point: 151°C.

Stability: Stable when stored at 0°C or lower as a solid. May oxidize slowly in solution.

Chemical reactivity: Hydrolyzes to the hydroxylamine in acidic or basic solution. Reacts with acid chlorides or acid anhydride to yield esters.

Flash point: No data.

Autoignition temperature: No data.

Flammable limits: No data.

, Explosion, and Reactivity Hazard Data

N-OH-AAF does not require special fire-fighting procedures or equipment and does not present unusual fire and explosion hazards. Because of the electrostatic nature of dry N-OH-AAF, fire fighters should wear full-face masks.

No conditions contributing to instability are known.

3. No incompatibilities have been reported.

4. No hazardous decomposition products are known.

5. N-OH-AAF does not require nonspark equipment. When handled in organic solvents, the precautions required for such solvents will apply.

Operational Procedures

The NIH Guidelines for the Laboratory Use of Chemical Carcinogens describe operational practices to be followed when potentially carcinogenic chemicals are used in NIH laboratories. The Guidelines should be consulted to identify the proper use conditions required and specific controls to be implemented during normal and complex operations or manipulations involving N-OH-AAF.

1. Chemical inactivation: No validated method reported.

2. Decontamination: Turn off equipment that could be affected by N-OH-AAF or the materials used for cleanup. If more than 1 g has been spilled or if there is any uncertainty regarding the procedures to be followed for decontamination, call the NIH Fire Department (dial 116) for assistance. Wipe off surfaces with acetone, then wash with copious quantities of water. Glassware should be rinsed (in a hood) with acetone, followed by soap and water. Animal cages should be washed with water.

3. Disposal: No waste streams containing N-OH-AAF shall be disposed of in sinks or general refuse. Surplus N-OH-AAF or chemical waste streams contaminated with N-OH-AAF shall be handled as hazardous chemical waste and disposed of in accordance with the NIH chemical waste disposal system. Nonchemical waste (e.g., animal carcasses and bedding) containing N-OH-AAF shall be handled and packaged for incineration in accordance with the NIH medical-pathological waste disposal system. Potentially infectious waste (e.g., tissue cultures) containing N-OH-AAF shall be disinfected by heat using a standard autoclave treatment and packaged for incineration, as above. Burnable waste (e.g., absorbent bench top liners) minimally contaminated with N-OH-AAF shall be handled as potentially infectious waste and packged for incineration, as above. Absorbent materials (e.g., associated with spill cleanup) grossly contaminated shall be handled in accordance with the chemical waste disposal system. Radioactive waste containing N-OH-AAF shall be handled in accordance with the NIH radioactive waste disposal system.

4. Storage: Store stock quantities of solid material or solutions in ampoules or screw-capped bottles or vials with Teflon cap liners. Storage at 0°C or lower improves stability. Avoid dispersal of electrostatically charged solid material while

Monitoring and Measurement Procedures Including Direct Field Measurements and Sampling for Subsequent Laboratory Analysis

Since N-OH-AAF is strictly a laboratory chemical, methods for field sampling and measurement have not been developed.

1. Sampling: N-OH-AAF may be extracted from biological material by organic solvents in neutral or weakly acid solution.

2. Separation and analysis: When necessary, N-OH-AAF can be separated from other constituents by GC (Bowman and King, 1974) or by HPLC (Fullerton and Jackson, 1976; Stanley et al., 1978) or TLC (Gutmann and Erickson, 1969, 1972) followed by UV spectrophotometry. A colorimetric method that is simpler but less specific is also available (Westfall and Morris, 1947).

Biological Effects (Animal and Human)

1. Absorption: N-OH-AAF is absorbed from the gastrointestinal tract and after parenteral administration.

2. Distribution: No data. By analogy with 2-acetylaminofluorene, it is probably incorporated into RNA and DNA of liver and other tissues.

3. Metabolism and excretion: The main site of metabolism is probably the liver, where it converts to electrophilic reactants, e.g., by sulfonation, to an "ultimate carcinogen." Hydroxylation of various positions of the ring system may also occur. Intraperitoneal injection of [9-^{14}C]N-OH-AAF results in excretio of 35-50% of the label in the urine and 20-25% in the feces within 24 hours, mostly as N- and ring-hydroxy AAF sulfates and glucuronides (Weisburger et al., 1964).

4. Toxic effects: The acute LD50 is 52 mg/kg (rat, intraperitoneal it is thus somewhat more toxic than 2-acetylaminofluorene. Chro administration results in liver damage.

5. Carcinogenic effects: Oral or parenteral administration of N-OH-AAF to rodents results in tumors primarily of the liver but also in the mammary gland, urinary bladder, and sebaceous glands of the ear duct. In addition, N-OH-AAF is carcinogenic at sites of application (e.g., skin, forestomach, subcutaneous injection site). In contrast to 2-aminofluorene and 2-acetylaminofluorene, the guinea pig is as susceptible as other rodent species to carcinogenicity due to N-OH-AAF.

6. Mutagenic and teratogenic effects: N-OH-AAF is a direct mutagen in bacterial systems, but its activity is enhanced by the presenc of an activating liver microsomal system. There are no data concerning its teratogenicity.

G. Emergency Treatment

1. Skin and eye exposure: For skin exposure, remove contaminated clothing and wash skin with soap and water. For eye exposure, irrigate immediately with copious quantities of running water for at least 15 minutes.

2. Ingestion: Drink plenty of water. Induce vomiting.

3. Inhalation: Remove victim promptly to clean air. Administer rescue breathing if necessary.

4. Refer to physician.

H. References

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Fullerton, F.R., and C.D. Jackson. 1976. Determination of 2-acetylaminofluorene and its metabolites in urine by high pressure liquid chromatography. Biochem Med 16:95-103.

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Gutmann, H.R., and R.R. Erickson. 1972. The conversion of the carcinogen N-hydroxy-2-fluorenylacetamide to o-amidophenols by rat liver in vitro: Substrate specificity and mechanism of the reaction. J Biol Chem 247:660-666.

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Westfall, B.B., and H.P. Morris. 1947. Photometric estimation of N-acetyl-2-aminofluorene. J Natl Cancer Inst 8:17-21.